WHAT IS CLAIMED:

1. A method for identifying one or more of a plurality of sequences differing by one or more single-base changes, insertions, deletions, or translocations in a plurality of target nucleotide sequences comprising:

providing a sample potentially containing one or more target nucleotide sequences with a plurality of sequence differences;

providing one or more oligonucleotide probe sets, each set characterized by (a) a first oligonucleotide probe, having a target-specific portion and a 5' upstream primer-specific portion and (b) a second oligonucleotide probe, having a target-specific portion and a 3' downstream primer-specific portion, wherein the oligonucleotide probes in a particular set are suitable for ligation together when hybridized adjacent to one another on a corresponding target nucleotide sequence, but have a mismatch which interferes with such ligation when hybridized to any other nucleotide sequence present in the sample;

providing a ligase;

blending the sample, the plurality of oligonucleotide probe sets, and the ligase to form a ligase detection reaction mixture;

subjecting the ligase detection reaction mixture to one or more ligase detection reaction cycles comprising a denaturation treatment, wherein any hybridized oligonucleotides are separated from the target nucleotide sequences, and a hybridization treatment, wherein the oligonucleotide probe sets hybridize at adjacent positions in a base-specific manner to their respective target nucleotide sequences, if present in the sample, and ligate to one another to form a ligation product sequence containing (a) the 5' upstream primer-specific portion, (b) the target-specific portions connected together, and (c) the 3' downstream primer-specific portion with the ligation product sequence for each set being distinguishable from other nucleic acids in the ligase detection reaction mixture, and, wherein the oligonucleotide probe sets may hybridize to nucleotide sequences

in the sample other than their respective target nucleotide sequences but do not ligate together due to a presence of one or more mismatches and individually separate during the denaturation treatment;

providing one or a plurality of oligonucleotide primer sets, each set characterized by (a) an upstream primer containing the same sequence as the 5' upstream primer-specific portion of the ligation product sequence and (b) a downstream primer complementary to the 3' downstream primer-specific portion of the ligation product sequence, wherein one of the primers has a detectable reporter label;

providing a polymerase;

blending the ligase detection reaction mixture with the one or a plurality of oligonucleotide primer sets, and the polymerase to form a polymerase chain reaction mixture;

subjecting the polymerase chain reaction mixture to one or more polymerase chain reaction cycles comprising a denaturation treatment, wherein hybridized nucleic acid sequences are separated, a hybridization treatment, wherein the primers hybridize to their complementary primer-specific portions of the ligation product sequence, and an extension treatment, wherein the hybridized primers are extended to form extension products complementary to the sequences to which the primers are hybridized, wherein, in a first cycle, the downstream primer hybridizes to the 3' downstream primer-specific portion of the ligation product sequence and extends to form an extension product complementary to the ligation product sequence, and, in subsequent cycles, the upstream primer hybridizes to the 5' upstream primer-specific portion of the extension product complementary to the ligation product sequence and the 3' downstream primer hybridizes to the 3' downstream portion of the ligation product sequence;

detecting the reporter labels; and

distinguishing the extension products to indicate the presence of one or more target nucleotide sequences in the sample.

2. A method according to claim 1, wherein one of the oligonucleotide probes in the set contains a restriction site, said method further comprising:

restriction digesting each extension product at the restriction sites to produce labelled extension product fragments, wherein the restriction site is positioned in each of the oligonucleotide probe sets to produce an extension product fragment with a unique length so that it can be distinguished from other nucleic acids in the polymerase chain reaction mixture after said restriction digesting; and

separating the extension product fragments by size or electrophoretic mobility, wherein said distinguishing differentiates the extension product fragments which differ in size.

3. A method according to claim 1, wherein the ligation product sequence of the oligonucleotide probes in a particular set produces an extension product of unique length so that it can be distinghished from other nucleic acids in the polymerase chain reaction mixture, said method further comprising:

separating the extension products by size or electrophoretic mobility, wherein said distinguishing differentiates the extension products which differ in size.

4. A method according to claim 1, wherein the oligonucleotides are configured so that the sequence of their ligation products across the ligation junction of each set is unique and can be distinguished from other nucleic acids in the polymerase chain reaction mixture, said method further comprising:

providing a solid support with different capture oligonucleotides immobilized at different particular sites, wherein the capture oligonucleotides have nucleotide sequences complementary to the unique nucleotide sequences across the ligation junctions of given probe sets;

contacting the polymerase chain reaction mixture, after said subjecting it to one or more polymerase chain reaction cycles, with the solid support under conditions effective to hybridize the extension products to the capture oligonucleotides in a base-specific manner, thereby capturing the extension products on the solid support at the site with the complementary capture oligonucleotide, wherein said detecting indicates the presence of extension products captured using the unique nucleotide sequence portions surrounding the ligation junction and immobilized to the solid support at particular sites, thereby indicating the presence of one or more target nucleotide sequences in the sample.

5. A method according to claim 1, wherein, in each primer set, one primer has a detectable reporter label and the other primer contains an addressable array-specific portion which is linked to the 5' end of that primer and remains single stranded after said subjecting the polymerase chain reaction mixture to one or more polymerase chain reaction cycles, said method further comprising:

providing a solid support with different capture oligonucleotides immobilized at different particular sites, wherein the capture oligonucleotides have nucleotide sequences complementary to the addressable array-specific portions;

contacting the polymerase chain reaction mixture, after said subjecting it to one or more polymerase chain reaction cycles, with the solid support under conditions effective to hybridize the extension products to the capture oligonucleotides in a base-specific manner, thereby capturing the addressable array-specific portions to the solid support at the site with the complementary capture oligonucleotide, wherein said detecting indicates the presence of extension products captured using the addressable array-specific portions and immobilized to the solid support at particular sites, thereby indicating the presence of one or more target nucleotide sequences in the sample.

6. A method according to claim 1, wherein the relative amounts of two or more of a plurality of sequences, differing by one or more single-base changes, insertions, deletions, or translocations and present in a sample in unknown amounts with a plurality of target nucleotide sequences being quantified and a set of oligonucleotide primers being useful in amplifying all the ligation product sequences formed by the oligonucleotide probe sets in a particular probe group, the oligonucleotide probe sets forming a plurality of oligonucleotide probe groups, each group comprised of two or more of the oligonucleotide probe sets, wherein oligonucleotide probe sets in the same group contain the same 5' upstream primer-specific portion and the same 3' downstream primer-specific portion, said method further comprising;

quantifying the relative amount of the extension products, after said distinguishing and

comparing relative amounts of the extension products generated to provide a quantitative measure of the relative level of the two or more target nucleotide sequences in the sample.

7. A method according to claim 6, wherein one of the oligonucleotide probes in each set contains a restriction site, said method further comprising:

restriction digesting the extension products at the restriction sites to produce labelled extension product fragments, wherein the restriction site is positioned in each of the oligonucleotide probe sets to produce an extension product fragment with a unique length so that it can be distinguished from other nucleic acids in the polymerase chain reaction mixture after said restriction digesting; and

separating the extension product fragments by size or electrophoretic mobility, wherein said distinguishing is carried out by size differences in the labeled extension product fragments.

8. A method according to claim 6, wherein oligonucleotide probe sets in the same group contain the same 5' upstream primer-specific portion and the same 3' downstream primer-specific portion, and the ligation product sequences of oligonucleotide probes in a particular set have a unique length product so that they can be distinguished from other nucleic acids in the polymerase chain reaction mixture, said method further comprising:

separating the extension products by size or electrophoretic mobility, wherein said detecting and said distinguishing are carried out by size differences in the labeled extension products.

9. A method according to claim 6, wherein the ligation product sequences of oligonucleotide probes in a particular set contain unique sequences across the ligation junction so that they can be distinguished from other nucleic acids in the polymerase chain reaction mixture, said method further comprising:

providing a solid support with different capture oligonucleotides immobilized at different particular sites, wherein the capture oligonucleotides have nucleotide sequences complementary to the unique nucleotide sequences across the ligation junctions of given probe sets;

contacting the polymerase chain reaction mixture, after said subjecting it to one or more polymerase chain reaction cycles, with the solid support under conditions effective to hybridize the extension products to the capture oligonucleotides in a base-specific manner, thereby capturing the extension products on the solid support at the site with the complementary capture oligonucleotide, wherein said detecting indicates the presence of extension products captured using the unique nucleotide sequence portions across the ligation junction and immobilized to the solid support at particular sites.

10. A method according to claim 1, wherein one or both oligonucleotide probes in a particular set have blocking groups at their non-ligating

ends with blocking group rendering the ligation product of the oligonucleotide probes in a particular set substantially resistant to exonuclease digestion, said method further comprising:

subjecting the ligase detection reaction mixture to exonuclease digestion after said subjecting the ligase detection reaction mixture to one or more ligase detection reaction cycles, wherein exonuclease substantially destroys oligonucleotide probes which are not blocked, does not destroy a substantial portion of the ligation products, and substantially reduces the presence of original target nucleotide sequences and

inactivating the exonuclease, wherein said subjecting to exonuclease digestion reduces formation of ligation independent extension products during said subjecting the polymerase chain reaction mixture to one or more polymerase chain reaction cycles.

11. A method according to claim 10, wherein the ligation product sequence of the oligonucleotide probes in a particular set generates a unique length product, said method further comprising:

separating the extension products by size or electrophoretic mobility, wherein said distinguishing differentiates the extension products which differ in size.

12. A method according to claim 11, wherein the one or more of a plurality of sequences differing by one or more single-base changes, insertions, deletions, or translocations are present in the sample in unknown amounts with a plurality of target nucleotide sequences being quantified, said method further comprising:

providing a known amount of one or more marker target nucleotide sequences;

providing one or a plurality of oligonucleotide probe groups, each group comprised of two or more of the oligonucleotide probe sets, including probe sets specifically designed for the marker target nucleotide sequences, wherein one or both oligonucleotide probes in a particular set are blocked at their non-ligating ends, wherein oligonucleotide probe sets in the same group contain either the same 5' upstream primer-specific portion or the same 3' downstream primer-specific portion, or both the same 5' upstream primer-specific portion and the same 3' downstream primer-specific portion, said ligase detection reaction mixture further comprising the marker target nucleotide sequences and the probe sets including probe sets specifically designed for the marker target nucleotide sequences, said method further comprising:

providing one or a plurality of oligonucleotide primer groups, each group comprised of two or more oligonucleotide primer sets, wherein the oligonucleotide primer sets in each group contain either the same 5' upstream primer or the same 3' downstream primer or both the same 5' upstream primer and the same 3' downstream primer, a group of oligonucleotide primers being useful to amplify all ligation product sequences in a given group;

quantifying the amount of extension products after said distinguishing; and

comparing the amounts of extension products generated from the unknown sample with the amount of extension products generated from known amounts of marker target nucleotide sequences to provide a quantitative measure of the level of one or more target nucleotide sequences in the sample.

13. A method according to claim 10, wherein one primer has a detectable reporter label and the other primer contains an addressable array-specific portion which is linked to the 5' end of that primer and rèmains single stranded after said subjecting the polymerase chain reaction mixture to one or more polymerase chain reaction cycles, said method further comprising:

providing a solid support with different capture oligonucleotides immobilized at different particular sites, wherein the capture oligonucleotides have nucleotide sequences complementary to the addressable array-specific portions;

contacting the polymerase chain reaction mixture, after said subjecting it to one or more polymerase chain reaction cycles, with the solid support under conditions effective to hybridize the extension products to the capture oligonucleotides in a base-specific manner, thereby capturing the addressable array-specific portions to the solid support at the site with the complementary capture oligonucleotide, wherein said detecting indicates the presence of extension products captured using the addressable array-specific portions and immobilized to the solid support at particular sites.

14. A method according to claim 13, wherein the one or more of a plurality of sequences differing by one or more single-base changes, insertions, deletions, or translocations are present in the sample in unknown amounts with a plurality of target nucleotide sequences being quantified, one primer has a detectable reporter label and the other primer contains an addressable array-specific portion which is linked to the 5' end of that primer and remains single stranded after said subjecting the polymerase chain reaction mixture to one or more polymerase chain reaction cycles, and the oligonucleotide primer sets in the same group contain either the same 5' upstream primer or the same 3' downstream primer, wherein a group of oligonucleotide primers may be used to amplify all ligation product sequences in a given group, said method further comprising:

providing a known amount of one or more marker target nucleotide sequences;

providing one or a plurality of oligonucleotide probe groups, each group comprised of two or more of the oligonucleotide probe sets, including

probe sets specifically designed for the marker target nucleotide sequences, wherein one or both oligonucleotide probe sets in the same group contain either the same 5' upstream primer-specific portion or the same 3' downstream primer-specific portion;

providing one or a plurality of oligonucleotide primer groups, each group comprised of two or more oligonucleotide primer sets, wherein the oligonucleotide primer sets in the same group contain either the same 5' upstream primer or the same 3' downstream primer and a group of oligonucleotide primers are used to amplify all ligation product sequences in a group;

blending the marker target nucleotide sequences and probe sets specifically designed for the marker target nucleotide sequences to the ligase detection reaction mixture;

quantifying the amount of extension products, and

comparing the amounts of extension products generated from the unknown sample with the amount of extension products generated from known amounts of marker target nucleotide sequences to provide a quantitative measure of the level of one or more target nucleotide sequences in the sample.

15. A method according to claim 1, wherein one or both oligonucleotide probes in a particular set contain deoxy-uracil in place of deoxy-thymidine with the deoxy-uracil rendering the oligonucleotide probes and their ligation product sequences substantially sensitive to uracil N-glycosylase, said method further comprising:

blending the ligase detection reaction mixture, after said subjecting the ligase detection reaction mixture to one or more ligase detection reaction cycles and before said subjecting the polymerase chain reaction mixture to one or more polymerase chain reaction cycles, with one or a plurality of the downstream primers complementary to the 3' downstream primer-specific portion

of the ligation product sequences, and the polymerase to form an extension mixture;

subjecting the extension mixture to a hybridization treatment, wherein the downstream primer hybridizes to the 3' downstream primer-specific portion of the ligation product sequence, and extends to form an extension product complementary to the ligation product sequence;

inactivating the polymerase;

blending the extension mixture, after said inactivating, with uracil N-glycosylase to form a uracil N-glycosylase digestion mixture;

subjecting the extension mixture to uracil-N-glycosylase digestion substantially to destroy oligonucleotide probes, ligation product sequences, and extension products off the original target which use the 5' upstream primer as primers, without destroying the 3' downstream primer extension product off the ligation product sequences;

inactivating the uracil N-glycosylase;

blending, after said inactivating the uracil N-glycosylase, a polymerase with the uracil N-glycosylase digestion mixture to form the polymerase chain reaction mixture;

subjecting the polymerase chain reaction mixture to the one or more polymerase chain reaction cycles to form an extension product in the first cycle which is substantially the same as the ligation product sequence except containing deoxy-thymidine in place of deoxy-uracil, and, in subsequent cycles, the 5' upstream primer hybridizes to the 5' upstream primer-specific portion of the extension product complementary to the ligation product sequence and the 3' downstream primer hybridizes to the 3' downstream portion of the extension product sequence which is substantially the same as the ligation product sequence, an extension treatment, whereby said subjecting the extension mixture to uracil N-glycosylase digestion substantially reduces the quantity of the ligation product sequences, either one or both oligonucleotide probes, and, thus, ligation

independent extension products from said subjecting the polymerase chain reaction mixture to one or more polymerase chain reaction cycles.

16. A method according to claim 15, wherein the ligation product sequences of oligonucleotide probes in a particular set generates a unique length product which is distinguishable from either probes or other ligation product sequence, said method further comprising:

separating the extension products by size or electrophoretic mobility, wherein said distinguishing differentiates the extension products which differ in size.

17. A method according to claim 16, wherein the one or more of a plurality of sequences differing by one or more single-base changes, insertions, deletions, or translocations are present in the sample in unknown amounts with a plurality of target nucleotide sequences being quantified, said method further comprising:

providing a known amount of one or more marker target nucleotide sequences:

providing one or more of marker-specific oligonucleotide probe sets, each set characterized by (a) a first oligonucleotide probe, having a target-specific portion and a 5' upstream primer-specific portion and (b) a second oligonucleotide probe, having a target-specific portion and a 3' downstream primer-specific portion, wherein one or both oligonucleotide probes in a particular set contain deoxy-uracil in place of deoxy-thymidine, wherein the oligonucleotide probes in a particular set are suitable for ligation together when hybridized adjacent to one another on a corresponding marker target nucleotide sequence, but, when hybridized to any other nucleotide sequence present in the sample or added marker sequences, have a mismatch which interferes with such ligation, said oligonucleotide probe sets and said marker-specific oligonucleotide sets forming a

plurality of oligonucleotide probe groups, wherein the ligation product sequence of oligonucleotide probes in a particular set generates a unique length product, and thus may be distinguished from either probes or other ligation product sequences in the same group or other groups;

blending the marker target nucleotide sequences and the probe sets specifically designed for the marker target nucleotide sequences with the ligase detection mixture;

providing one or a plurality of oligonucleotide primer groups, each group comprised of two or more of the oligonucleotide primer sets, wherein oligonucleotide primer sets in the same group contain either the same 5' upstream primer or the same 3' downstream primer, or both the same 5' upstream primer and the same 3' downstream primer, wherein a group of oligonucleotide primers may be used to amplify all the ligation product sequences in a given group;

separating the extension products by size or electrophoretic mobility;

quantifying the amount of extension products after said distinguishing; and

comparing the amounts of extension products generated from the unknown sample with the amount of extension products generated from known amounts of marker target nucleotide sequences to prove a quantitative measure of the level of one or more target nucleotide sequences in the sample.

18. A method according to claim 15, wherein, in each primer set, one primer has a detectable reporter label and the other primer contains an addressable array-specific portion which is linked to the 5' end of that primer and remains single stranded after said subjecting the polymerase chain reaction mixture of one or more polymerase chain reaction cycles, said method further comprising:

providing a solid support with different capture oligonucleotides immobilized at different particular sites, wherein the capture oligonucleotides have nucleotide sequences complementary to the array-specific portions and

contacting the polymerase chain reaction mixture, after said subjecting it to one or more polymerase chain reaction cycles, with the solid support under conditions effective to hybridize the extension products to the capture oligonucleotides in a base-specific manner, thereby capturing the addressable array-specific portions to the solid support at the site with the complementary capture oligonucleotide, wherein said detecting indicates the presence of extension products captured using the addressable nucleotide sequence portions and immobilized to the solid support at particular sites.

19. A method according to claim 18, wherein the one or more of a plurality of sequences differing by one or more single-base changes, insertions, deletions, or translocations are present in the sample in unknown amounts with a plurality of target nucleotide sequences being quantified, said method further comprising:

providing a known amount of one or more marker target nucleotide sequences;

providing one or a plurality of oligonucleotide probe groups, each group comprised of two or more of the oligonucleotide probe sets, including probe sets specifically designed for the marker target nucleotide sequences, wherein the ligation product sequences of oligonucleotide probes in a particular set may be distinguished from either probes or other ligation product sequences in the same group or other groups;

blending the marker target nucleotide sequences and the probe sets specifically designed for the marker target nucleotide sequences with the ligase detection mixture;

providing one or a plurality of oligonucleotide primer groups, each group comprised of two or more of the oligonucleotide primer sets, wherein oligonucleotide primer sets in the same group contain either the same 5' upstream primer or the same 3' downstream primer, wherein a group of oligonucleotide primers may be used to amplify all ligation product sequences in a given group;

quantifying the amount of extension products; and

comparing the amounts of extension products generated from the unknown sample with the amount of extension products generated from known amounts of marker target nucleotide sequences to provide a quantitative measure of the level of one or more target nucleotide sequences in the sample.

20. A method according to claim 1, wherein each of the denaturation treatments is at a temperature of about 80°-105°C.

21. A method according to claim 1, wherein each cycle of the ligase detection reaction, comprising a denaturation treatment and a hybridization treatment, is from about 30 seconds to about five minutes long.

22. A method according to claim 1, wherein said subjecting the ligase detection reaction mixture to one or more ligase detection reaction cycles is repeated for 2 to 50 cycles.

23. A method according to claim 1, wherein total time for said subjecting the ligase detection reaction mixture to one or more ligase detection reaction cycles is 1 to 250 minutes.

24. A method according to claim 1, wherein the ligase is selected from the group consisting of *Thermus aquaticus* ligase, *Thermus thermophilus* ligase, *E. coli* ligase, T4 ligase, and *Pyrococcus* ligase.

25. A method according to claim 1, wherein the detectable reporter label is selected from the group consisting of chromophores, fluorescent moieties, enzymes, antigens, heavy metals, magnetic probes, dyes, phosphorescent groups, radioactive materials, chemiluminescent moieties, and electrochemical detecting moieties.

26. A method according to claim 1, wherein the target-specific portions of the oligonucleotide probes each have a hybridization temperature of 50-85°C.

27. A method according to claim 1, wherein the target-specific portions of the oligonucleotide probes are 20 to 28 nucleotides long.

28. A method according to claim 1, wherein the oligonucleotide probe sets are selected from the group consisting of ribonucleotides, deoxyribonucleotides, modified ribonucleotides, modified deoxyribonucleotides, modified phosphate-sugar backbone oligonucleotides, nucleotide analogues, and mixtures thereof.

29. A method for identifying two or more of a plurality of sequences differing by one or more single-base changes, insertions, deletions, or translocations in a plurality of target nucleotide sequences comprising:

providing a sample potentially containing one or more target nucleotide sequences with a plurality of sequence differences;

providing one or more of primary oligonucleotide primer groups, each group comprised of one or more primary oligonucleotide primer sets, each set characterized by (a) a first oligonucleotide primer, having a target-specific portion and a 5' upstream secondary primer-specific portion, and (b) a second oligonucleotide primer, having a target-specific portion and a 5' upstream secondary primer-specific portion, wherein the first oligonucleotide primers of each set in the same group contain the same 5' upstream secondary primer-specific portion and the second oligonucleotide primers of each set in the same group contain the same 5' upstream secondary primer-specific portion, wherein the oligonucleotide primers in a particular set are suitable for hybridization on complementary strands of a corresponding target nucleotide sequence to permit formation of a polymerase chain reaction product, but have a mismatch which interferes with formation of such a polymerase chain reaction product when hybridized to any other nucleotide sequence present in the sample, and wherein the polymerase chain reaction products in a particular set may be distinguished from other polymerase chain reaction products in the same group or other groups;

providing a polymerase;

blending the sample, the primary oligonucleotide primers, and the polymerase to form a primary polymerase chain reaction mixture;

subjecting the primary polymerase chain reaction mixture to two or more polymerase chain reaction cycles comprising a denaturation treatment, wherein hybridized nucleic acid sequences are separated, a hybridization treatment, wherein the target-specific portions of the primary oligonucleotide primers hybridize to the target nucleotide sequences, and an extension treatment, wherein the hybridized primary oligonucleotide primers are extended to form primary extension products complementary to the target nucleotide sequence to which the primary oligonucleotide primer is hybridized;

providing one or a plurality of secondary oligonucleotide primer sets, each set characterized by (a) a first secondary primer containing the

same sequence as the 5' upstream portion of a first primary oligonucleotide primer, and (b) a second secondary primer containing the same sequence as the 5' upstream portion of a second primary oligonucleotide primer from the same primary oligonucleotide primer set as the first primary oligonucleotide contained by the first secondary primer, wherein a set of secondary oligonucleotide primers may be used to amplify all of the primary extension products in a given group;

blending the primary extension products, the secondary oligonucleotide primers, and the polymerase to form a secondary polymerase chain reaction mixture;

subjecting the secondary polymerase chain reaction mixture to two or more polymerase chain reaction cycles comprising a denaturation treatment, wherein hybridized nucleic acid sequences are separated, a hybridization treatment, wherein the secondary oligonucleotide primers hybridize to the primary extension products, an extension treatment, wherein the hybridized secondary oligonucleotide primers are extended to form secondary extension products complementary to the primary extension products;

providing a plurality of oligonucleotide probe sets, each set characterized by (a) a first oligonucleotide probe, having a secondary extension product-specific portion and a detectable reporter label, and (b) a second oligonucleotide probe, having a secondary extension product-specific portion, wherein the oligonucleotide probes in a particular set are suitable for ligation together when hybridized adjacent to one another on a complementary secondary extension product-specific portion, but have a mismatch which interferes with such ligation when hybridized to any other nucleotide sequence present in the sample;

providing a ligase;

blending the secondary extension products, the plurality of oligonucleotide probe sets, and the ligase to form a ligase detection reaction mixture;

subjecting the ligase detection reaction mixture to one or more ligase detection reaction cycles comprising a denaturation treatment, wherein any hybridized oligonucleotides are separated from the secondary extension product, and a hybridization treatment, wherein the oligonucleotide probe sets hybridize at adjacent positions in a base-specific manner to their respective secondary extension products, if present, and ligate to one another to form a ligation product sequence containing (a) the detectable reporter label and (b) the secondary extension product-specific portions connected together, wherein the oligonucleotide probe sets may hybridize to nucleotide sequences other than their respective complementary secondary extension products but do not ligate together due to a presence of one or more mismatches and individually separate during the denaturation treatment; and

detecting the reporter labels of the ligation product sequences, thereby indicating the presence of two or more target nucleotide sequences in the sample.

30. A method according to claim 29, wherein the ligation product sequences of the oligonucleotide probes in a particular set have a unique length so that they can be distinguished from other nucleic acids in the ligase detection reaction mixture, said method further comprising:

separating the ligation product sequences by size or electrophoretic mobility and

distinguishing, after said detecting, the ligation product sequences which differ in size.

31. A method according to claim 29, wherein the second oligonucleotide probe of each set has an addressable array-specific portion, said method further comprising:

providing a solid support with different capture oligonucleotides immobilized at different particular sites, wherein the capture oligonucleotides have nucleotide sequences complementary to the addressable array-specific portions and

contacting the ligase detection reaction mixture, after said subjecting it to one or more ligase detection reaction cycles, with the solid support under conditions effective to hybridize the ligation product sequences to the capture oligonucleotides in a base-specific manner, thereby capturing the addressable array-specific portions to the solid support at the site with the complementary capture oligonucleotide, wherein said detecting indicates the presence of ligation product sequences captured using the addressable array-specific portions and immobilized to the solid support at particular sites, thereby indicating the presence of one or more target nucleotide sequences in the sample.

32. A method according to claim 29, wherein the relative amounts of one or more of a plurality of sequences, differing by one or more single-base changes, insertions, deletions, or translocations and present in a sample in unknown amounts with one or more target nucleotide sequences being quantified, said method further comprising:

quantifying, after said subjecting the secondary polymerase chain reaction mixture to one or more polymerase chain reaction cycles, the amounts of secondary extension products;

providing a known amount of one or more marker target nucleotide sequences;

providing one or more sequence-specific probe sets, including probe sets specifically designed for the marker target nucleotide sequences;

blending the marker target nucleotide sequences, and the probe sets specifically designed for the marker target nucleotide sequences with ligase detection reaction mixture;

quantifying the amount of ligation product sequences; and

comparing the amount of ligation product sequences generated from the unknown sample with the amount of ligation product sequences generated from known amounts of marker target nucleotide sequences to provide a quantitative measure of the relative level of one or more target nucleotide sequences in the sample.

33. A method according to claim 32, wherein the second oligonucleotide probe has an addressable array-specific portion, said method further comprising:

providing a solid support with different capture oligonucleotides immobilized at different particular sites, wherein the capture oligonucleotides have nucleotide sequences complementary to the addressable array-specific portions;

contacting the ligase detection reaction mixture, after said subjecting it to one or more ligase detection reaction cycles, with the solid support under conditions effective to hybridize the ligation product sequences to the capture oligonucleotides in a base-specific manner, thereby capturing the addressable array-specific portions to the solid support at the site with the complementary capture oligonucleotide; and

quantifying the amount of ligation product sequences captured using the addressable array-specific portions and immobilized to the solid support at particular sites;

comparing the amount of captured ligation product sequences generated from the unknown sample with the amount of captured ligation product sequences generated from known amounts of marker target nucleotide sequences to

provide a quantitative measure of the relative level of two or more target nucleotide sequences in the sample.

34. A method according to claim 32, wherein the one or more marker target nucleotide sequences differ from the target nucleotide sequences at one or more single nucleotide positions.

35. A method according to claim 32, wherein the oligonucleotide probe sets form a plurality of oligonucleotide probe groups, each group comprised of one or more oligonucleotide probe sets designed for distinguishing multiple allele differences at a single nucleotide position, wherein, in the oligonucleotide probe sets of each group, there is a common first oligonucleotide probe, having a secondary extension product-specific portion and a detectable reporter label, and a second oligonucleotide probe, having a secondary extension product-specific portion which hybridizes to a given allele or marker nucleotide sequence in a base-specific manner, each second oligonucleotide probe having a different length and, wherein the ligation product sequences of oligonucleotide probes in a particular set generate a unique length product, said method further comprising:

separating the ligation product sequences by size or electrophoretic mobility and

distinguishing the ligation product sequences which differ in size.

36. A method according to claim 32, wherein the oligonucleotide probe sets form a plurality of oligonucleotide probe groups, each group comprised of one or more oligonucleotide probe sets designed for distinguishing multiple allele differences at a single nucleotide position, wherein, in the oligonucleotide probe sets of each group, there is a common first oligonucleotide probe, having a secondary extension product-specific portion, and a second oligonucleotide probe,

having a secondary extension product-specific portion which hybridizes to a given allele or marker nucleotide sequence in a base-specific manner, each second oligonucleotide probe having a different detectable reporter label and wherein the ligation product sequences of oligonucleotide probes in a particular set generate a unique length product. said method further comprising:

separating the ligation product sequences by size or electrophoretic mobility and

distinguishing the ligation product sequences which differ in size.

37. A method according to claim 33, wherein the oligonucleotide probe sets form a plurality of oligonucleotide probe groups, each group comprised of one or more oligonucleotide probe sets designed for distinguishing multiple allele differences at a single nucleotide position, wherein, in the oligonucleotide probe sets of each group, there is a common first oligonucleotide probe, having a secondary extension product-specific portion and a detectable reporter label and a second oligonucleotide probe having a secondary extension product-specific portion which hybridizes to a given allele or a marker nucleotide sequence in a base-specific manner, each second oligonucleotide probe each having different addressable array-specific portions.

38. A method according to claim 33, wherein the oligonucleotide probe sets form a plurality of oligonucleotide probe groups, each group comprised of one or more oligonucleotide probe sets designed for distinguishing multiple allele differences at a single nucleotide position, wherein, in the oligonucleotide probe set of each group, there is a common first oligonucleotide probe, having a secondary extension product-specific portion and an addressable array-specific portion, and a second oligonucleotide probe, having a secondary extension product-specific portion which hybridizes to a given allele or a marker nucleotide

sequence in a base-specific manner, each second oligonucleotide probe having different detectable reporter label.

39. A method according to claim 29, wherein multiple allele differences at two or more nearby or adjacent nucleotide positions in a single target nucleotide sequence or multiple allele differences at two or more nearby or adjacent nucleotide positions in multiple target nucleotide sequences are distinguished with oligonucleotide probe sets having secondary extension-specific portions which may overlap.

40. A method according to claim 29, wherein a low abundance of multiple allele differences at multiple nearby or adjacent positions in a single target nucleotide sequence in the presence of an excess of normal sequence. or a low abundance of multiple allele differences at multiple nearby positions in multiple target nucleotide sequences in the presence of an excess of normal sequence in a sample are distinguished, the oligonucleotide probe set forming a plurality of oligonucleotide probe groups, each group comprised of one or more oligonucleotide probe sets designed for distinguishing multiple allele differences at a single nucleotide position, wherein one or more sets within a group share common first oligonucleotide probes, and the second oligonucleotide probes have secondary extension product-specific portions, which hybridize to a given allele excluding the normal allele in a base-specific manner, wherein, in said detecting, the labels of ligation product sequences are detected, thereby indicating a presence, in the sample, of one or more low abundance alleles at one or more nucleotide positions in one or more target nucleotide sequences.

41. A method according to claim 29, wherein a low abundance of multiple allele differences at multiple nearby or adjacent positions in a single target nucleotide sequence, in the presence of an excess of normal sequence, or a

low abundance of multiple allele differences at multiple nearby positions in multiple target nucleotide sequences, in the presence of an excess of normal sequence, in the sample in unknown amounts are quantified, said method further comprising:

providing a known amount of one or more marker target nucleotide sequences;

providing one or more marker-specific oligonucleotide probe sets, each set characterized by (a) a first oligonucleotide probe having a target-specific portion complementary to a marker target nucleotide sequence and (b) a second oligonucleotide probe, having a target-specific portion complementary to a marker target nucleotide sequence and a detectable reporter label, wherein the oligonucleotide probes in a particular marker-specific oligonucleotide set are suitable for ligation together when hybridized adjacent to one another on a corresponding marker target nucleotide sequence, but, when hybridized to any other nucleotide sequence present in the sample or added marker sequences, have a mismatch which interferes with such ligation, wherein said plurality of oligonucleotide probe sets and said plurality of marker-specific oligonucleotide probe sets form oligonucleotide probe groups for distinguishing multiple allele differences at a single nucleotide position, including marker nucleotide sequences, wherein one or more sets within a group share a common first oligonucleotide probe and a second oligonucleotide probe, having a secondary extension product-specific portion, which hybridizes to a given allele excluding the normal allele in a base-specific manner, wherein said blending to form the ligase detection reaction mixture comprises blending the marker target nucleotide sequences and the probe sets specifically designed for the marker target nucleotide sequences with the ligase detection reaction mixture;

quantifying the amount of ligation product sequences; and

comparing the amount of ligation product sequences generated from the low abundance unknown sample with the amount of ligation

product sequences generated from known amounts of marker target nucleotide sequences, to provide a quantitative measure of the level of one or more low abundance target nucleotide sequences in the sample.

42. A method according to claim 29, wherein each of the denaturation treatments is at a temperature of about 80°-105°C.

43. A method according to claim 29, wherein each cycle of the ligase detection reaction, comprising a denaturation treatment and a hybridization treatment, is from about 30 seconds to about five minutes long.

44. A method according to claim 29, wherein said subjecting the ligase detection reaction mixture to one or more ligase detection reaction cycles is repeated for 2 to 50 cycles.

45. A method according to claim 29, wherein the total time for said subjecting the ligase detection reaction mixture to one or more ligase detection reaction cycles is 1 to 250 minutes.

46. A method according to claim 29, wherein the ligase is selected from the group consisting of *Thermus aquaticus* ligase, *Thermus thermophilus* ligase, *E. coli* ligase, T4 ligase, and *Pyrococcus* ligase.

47. A method according to claim 29, wherein the detectable reporter label is selected from the group consisting of chromophores, fluorescent moieties, enzymes, antigens, heavy metals, magnetic probes, dyes, phosphorescent groups, radioactive materials, chemiluminescent moieties, and electrochemical detecting moieties.

48. A method according to claim 29, wherein the target-specific portions of the oligonucleotide probes each have a hybridization temperature of 50-85°C.

49. A method according to claim 29, wherein the target-specific portions of the oligonucleotide probes are 20 to 28 nucleotides long.

50. A method according to claim 29, wherein the oligonucleotide probe sets are selected from the group consisting of ribonucleotides, deoxyribonucleotides, modified ribonucleotides, modified deoxyribonucleotides, modified phosphate-sugar backbone oligonucleotides, nucleotide analogues, and mixtures thereof.

51. A method for identifying two or more of a plurality of sequences differing by one or more single-base changes, insertions, deletions, or translocations in a plurality of target nucleotide sequences comprising:

providing a sample potentially containing one or more target nucleotide sequences with a plurality of sequence differences;

providing one or more primary oligonucleotide primer groups, each group comprised of one or more primary oligonucleotide primer sets, each set characterized by (a) a first oligonucleotide primer, having a target-specific portion and a 5' upstream secondary primer-specific portion, and (b) a second oligonucleotide primer, having a target-specific portion and a 5' upstream secondary primer-specific portion, wherein the first oligonucleotide primers of each set in the same group contain the same 5' upstream secondary primer-specific portion and the second oligonucleotide primers of each set in the same group contain the same 5' upstream secondary primer-specific portion, wherein the oligonucleotide primers in a particular set are suitable for hybridization on complementary strands of a corresponding target nucleotide sequence to permit

formation of a polymerase chain reaction product, but have a mismatch which interferes with formation of such a polymerase chain reaction product when hybridized to any other nucleotide sequence present in the sample, and wherein the polymerase chain reaction products in a particular set may be distinguished from other polymerase chain reaction products in the same group or other groups;

providing a polymerase;

blending the sample, the primary oligonucleotide primers, and the polymerase to form a primary polymerase chain reaction mixture;

subjecting the primary polymerase chain reaction mixture to two or more polymerase chain reaction cycles comprising a denaturation treatment, wherein hybridized nucleic acid sequences are separated, a hybridization treatment, wherein the target-specific portion of the primary oligonucleotide primers hybridize to the target nucleotide sequences, and an extension treatment, wherein the hybridized primary oligonucleotide primers are extended to form primary extension products complementary to the target nucleotide sequence to which the primary oligonucleotide primer is hybridized;

providing one or a plurality of secondary oligonucleotide primer sets, each set characterized by (a) a first secondary primer, having a detectable reporter label and containing the same sequence as the 5' upstream portion of a first primary oligonucleotide primer, and (b) a second secondary primer containing the same sequence as the 5' upstream portion of a second primary oligonucleotide primer from the same primary oligonucleotide primer set as the first primary oligonucleotide complementary to the first secondary primer, wherein a set of secondary oligonucleotide primers amplify the primary extension products in a given group;

blending the primary extension products, the secondary oligonucleotide primers, and the polymerase to form a secondary polymerase chain reaction mixture;

subjecting the secondary polymerase chain reaction mixture to two or more polymerase chain reaction cycles comprising a denaturation treatment, wherein hybridized nucleic sequences are separated, a hybridization treatment, wherein the secondary oligonucleotide primers hybridize to the primary extension products, an extension treatment, wherein the hybridized secondary oligonucleotide primers are extended to form secondary extension products complementary to the primary extension product; and

detecting the labeled secondary extension products, thereby indicating the presence of one or more target nucleotide sequences in the sample.

52. A method according to claim 51, wherein the polymerase chain reaction secondary oligonucleotide primers in a particular set produce secondary extension products of unique length so that they may be distinguished from other nucleic acids in the secondary polymerase chain reaction mixture, said method further comprising:

separating the extension products by size or electrophoretic mobility and

distinguishing the secondary extension products which differ in size.

53. A method according to claim 51, wherein the secondary extension products contain unique sequences so that they may be distinguished from other secondary extension products, said method further comprising:

providing a solid support with different capture oligonucleotides immobilized at different particular sites, wherein the capture oligonucleotides have nucleotide sequences complementary to the unique nucleotide sequences within the secondary extension products;

contacting the secondary polymerase chain reaction mixture, after said subjecting it to one or more polymerase chain reaction cycles, with the solid support under conditions effective to hybridize the secondary extension

products to the capture oligonucleotides in a base-specific manner, thereby capturing the secondary extension products to the solid support at the site with complementary capture oligonucleotides, wherein said detecting indicates the presence of secondary extension products captured using the unique nucleotide sequence portions within the secondary extension products and immobilized to the solid support at particular sites, thereby indicating the presence of one or more target nucleotide sequences in the sample.

54. A method according to claim 51, wherein the primary oligonucleotide primer sets in the same group contain either the same 5' upstream primer-specific portion on the first oligonucleotide primers or the same 5' upstream primer-specific portion on the second oligonucleotide primers and, the secondary oligonucleotide primer sets form one or a plurality of oligonucleotide primer groups, each group comprised of one or more oligonucleotide primer sets, wherein one secondary oligonucleotide primer has a detectable reporter label and the other secondary oligonucleotide primer contains an addressable array-specific portion linked to the 5' end of that primer which remains single stranded after said subjecting the secondary polymerase chain reaction mixture to one or more polymerase chain reaction cycles, the oligonucleotide primer sets in the same group contain either the same first secondary oligonucleotide primer or the same second secondary oligonucleotide primer, wherein a group of secondary oligonucleotide primers may be used to amplify all the primary extension products in a given groups, said method further comprising:

providing a solid support with different capture oligonucleotides immobilized at different particular sites, wherein the capture oligonucleotides have nucleotide sequences complementary to the addressable array-specific portions;

contacting the secondary polymerase chain reaction mixture, after said subjecting it to one or more polymerase chain reaction cycles, with the

solid support under conditions effective to hybridize the secondary extension products to the capture oligonucleotides in a base-specific manner, thereby capturing the addressable array-specific portions to the solid support at the site with the complementary capture oligonucleotide, wherein said detecting indicates the presence of extension products captured using the addressable array-specific portions and immobilized to the solid support at particular sites, thereby indicating the presence of one or more target nucleotide sequences in the sample.